FILE NAME: New York State & NY Times (NY)

DATE: 1950 Apr

DOC#: NY100

DOCUMENT DESCRIPTION: NY Dept of Labor Monthly Review - Occupational Causes of Cancer

New York State Department of Labor

MONTHLY REVIEW

Division of Industrial Hygiene & Safety Standards

Vol. 29 April, 1950 No. 4

OCCUPATIONAL CAUSES OF CANCER*

MAY R. MAYERS, M.D.**
Chief, Medical Unit

The most interesting thing about occupational causes of cancer is how little we know about them. On the other hand, what we do know is truly provocative in that we can actually produce cancer at specific sites in the body, by known chemical agents, as a result of exposure in industry. This is particularly remarkable in view of the continued lack of knowledge of the basic causes of cancer, in general. It should some day fall into its appropriate niche in the large mosaic now being built up piecemeal by independent contributions from the research work of scientific investigators in many fields. Furthermore, the problems involved in developing new data are sufficiently complex to present a major challenge to any research worker with sufficient curiosity and imagination.

In New York State, the Division of Industrial Hygiene has had considerable experience with many facets of this problem, including the control of known carcinogens in industry and an attempt to develop new data. But before going into this, it might be well to survey, briefly, what is actually known and what is being conjectured at the present time with reference to occupational causes of cancer; and to bring to your attention the need for further evidence in the case of many substances or conditions in the occupational environment which are now suspect, but concerning which all too little is known.

As background material, it might be well to consider briefly the nature of the occupational environment as a whole; the abnormal elements in this environment which may give rise to occupational diseases generally, including occupational cancer and some of the techniques for their evaluation and control.

The more one knows about the industrial environment, the more one is impressed with its complexity. It is, after all, a man-made environment in which each worker is exposed to chemical substances and conditions peculiar to his workroom; an environment which is quite different from that of his family or his neighbors. Aside from dangerous machinery, which contributes by far the highest toll of injury to health in the form of industrial accidents, there are the more subtle health hazards which arise from exposure to a variety of special circumstances, such as the presence in the working environment of atmospheric contaminants in the form of dusts, gases, fumes, vapors or mists; radiation; excessive noise; improper illumination; continual vibration; abnormalities in temperature, humidity or air pressure, and so forth.

Has it ever occurred to you that inhalation of dust is not necessarily associated with pneumoconiosis? When industrial dusts are being considered, one usually thinks only in terms of such substances as silica or asbestos, which give rise to characteristic lung pathology; and attention is usually focused, therefore, upon x-ray diagnosis, particle size, dust counts and dust counting techniques. That these considerations do not apply to a great variety of the dusts to which workers are exposed in industry, is often overlooked.

When lead dust is inhaled, for example, it is dissolved in alveolar fluids and carried in the blood stream to all parts of the body, producing the rather complex systemic disease known as lead poisoning. Flour dust, on the other hand, acts as a sensitizing agent, which in *extremely* minute amounts is capable of producing asthma or other manifestations of allergy in susceptible individuals. Zinc fumes are precipitated on mucous surfaces as fine particles of zinc oxide, and as such give rise to transient anaphylactic reactions. In the case of other so-called "non-specific" dusts such as wood, fertilizer, methyl methacrylate plastics and so on, one is dealing primarily not with lung pathology but with irritation of the upper respiratory passages, or interference with normal ciliary and physiological function of mucous membranes. Standard dust counting techniques are not applicable to most of these dusts and standards for permissible dust counts do not exist, excepting in the most general terms.

Among the gases, the colorless, odorless, tasteless and non-irritating carbon monoxide may cause

* Presented at Graduate Course on Industrial Medicine under auspices of Academy of Compensation Medicine, University Hospital, New York City, Mar. 3, 1950.

** Chairman, New York State Occupational Cancer Committee.

MONTHLY REVIEW
of the
DIVISION OF INDUSTRIAL HYGIENE
AND SAFETY STANDARDS
NEW YORK STATE
DEPARTMENT OF LABOR
80 CENTRE STREET
NEW YORK 13, N. Y.
Industrial Commissioner
EDWARD CORSI
1st Deputy Industrial Commissioner
THOMAS F. MOORE, JR.
Deputy Industrial Commissioner in Charge
EDWARD A. NYEGAARD
Deputy Industrial Commissioner
ABRHAM H. GOODMAN
The Division
LEONARD GREENBURG, M.D., Director
MAY R. MAYERS, M.D., Medical Unit
WILLIAM J. BURKE, Chemical Unit
GEORGE P. KEOGH, Code Unit
ARTHUR C. STERN, Engineering Unit
Industrial Hygiene
LEONARD A. PERRIN, Engineering Unit
Building Plans

death by tissue asphyxia; or in lesser concentrations, it will give rise to varying degrees of anoxemia, depending upon the amounts of oxygen displaced from the hemoglobin molecules of red blood cells. Hydrogen cyanide also causes tissue asphyxia, but by a totally different mechanism—its interference with their oxygen receptors so that, while ample oxygen is available, tissue cells cannot utilize it. Highly irritant gases, such as ammonia, do not often present a serious health hazard because no one will usually remain in its presence long enough to be injured. When a pipe line breaks accidentally, however, and workers cannot be evacuated fast enough, pneumonia or edema of the lungs may ensue. It is the nitrous fumes, however, from welding operations in enclosed spaces which are peculiarly insidious. For, while they appear to be entirely innocuous during the time of exposure, sudden death from acute edema of the lungs may occur quite unexpectedly after a latent period of 8, 10 or 12 hours, during which time the worker usually does not usually feel sick.

Among the volatile solvents are those which have a special affinity for the hemapoetic system, such as benzol; those which may cause characteristic injury to the liver, such as carbon tetrachloride or the chlorinated diphenyls; those which primarily affect the nervous systm, such as trichlorethylene, which in ordinary use may act merely as a narcotic, or carbon disulphide, which in sufficient concentration is capable of causing abnormal behavior patterns largely indistinguishable from non-occupational psychoneuroses and psychoses. It is largely a matter of dosage what the toxicological effects will be, or whether there will be any adverse effects at all.

In skin contact with chemicals, equally complex and varied mechanisms are involved. Some chemicals are caustic or act as primary irritants. Others, such as paraphenylene diamine, a common fur dye, may act only as sensitizing agents. Still others, such as nicotine, for example, may be absorbed through the skin to produce systemic disease. The chlorinated naphthalenes produce typical acne form lesions of the skin; certain heavy oils and tars are carcinogenic.

For purposes of control, maximum allowable concentrations have been developed for exposure to chemical substances or abnormal environmental conditions in industry; and techniques have been developed for evaluating these exposures to determine whether safe limits have been exceeded in a particular workroom or plant operation. Unfortunately, such standards are not a guide to the control of carcinogenic agents in industry, since there is no known relationship between the toxicological properties of a substance and its carcinogenic potentialities. Beta naphthylamine, for example, which is a well established carcinogen, even in small amounts, has not been shown to produce systemic disease generally. Control of carcinogenic agents in industry, moreover, is difficult because cancer takes so many years to develop that control measures must be operative for a long period of time before their effectiveness can be evaluated.

As a means of illuminating the occupational cancer problem from still another angle, it might be profitable to consider some of the other characteristics of the occupational environment, and some of the special medical problems to which they give rise. First of all, exposure is such as to rarely cause acute illness or death. The more usual situation is that of continuous or intermittent exposure to relatively low concentrations of toxic chemicals or low dosage of other adverse environmental conditions for relatively long periods of time. Medically, therefore, the situation may be puzzling. One does not necessarily see clearly defined chemical disease entities or frank disability in most cases. Often, they carry no earmarks whatever of their occupational origin, as in the case of hepatitis, aplastic anemia or bladder cancer. Delayed onset, after the pertinent exposure has ceased, not only occurs in connection with occupational cancer but has been found in aplastic anemia due to benzol as well.

The fact that labor is mobile, and workers go from job to job where environmental exposures differ, creates further difficulties for the physician. This is true especially in the older worker who, in the course of a long life, has developed many pathological and functional changes in various tissues or organs of his body. His doctor is usually capable of evaluating the usual signs of aging or of intercurrent disease. However, in the case of a worker who has spent many years of his life exposed to even a single toxic chemical, such as lead, for example, the medical practitioner finds himself put to it all along the line to dissociate those elements in the clinical picture which may properly be attributed to the lead, from those which are due to the aging process or other unrelated conditions.

In industry one may be dealing with cumulative poisons, such as lead or mercury; or with cumulative pathology, as in the case of a liver which has been exposed to repeated insults by hepatotoxic substances until its regenerative powers have been overwhelmed and evidences of liver insufficiency begin to make their appearance; or acute yellow atrophy causes the death of the worker. The liver is, indeed, a focal point in all exposures to toxic chemicals, in that it is *the* de-toxifying organ in the body. One can raise an interesting question,

effectiveness of different research techniques.

One approach is the use of death certificates, noting the occupation given. Social Security records—which now cover the last ten years—make it possible to check back on previous occupations for this ten-year period. One can take a suspected industry or plant and try to follow back, by means of social security numbers, workers who had left the plant and subsequently died of cancer. One can compare the cancer incidence rate of communities in which suspected carcinogens are present in the industries with that of similar communities not having such plants. One can study the effects of air pollution by industrial plants in a community or in a given geographic area upon the cancer incidence in that area. One can interview cancer patients and get detailed occupational histories going back to each patient's first job.

Each of these methods has merit. Each also has its limitations. Interviewing cancer patients for the purpose of obtaining reliable occupational histories and accurate technical data as to the occupational exposures associated with each job is not only time-consuming, but requires an industrial hygiene valuation of each interview. Official records, on the other hand, are notably lacking in precise and pertinent information with reference to the occupational exposure. And yet, there are many situations where there is no alternative, since they provide information which cannot be obtained in any other way.

The use of death certificates, for example, is limited primarily by the fact that only the last occupation is given, whereas occupational cancer is more apt to have been caused by some previous occupational exposure, perhaps ten or fifteen years earlier. Moreover, death certificates indicate only those persons who actually died of cancer. They do not include patients who had recovered, and who subsequently died of one or another unrelated condition, such as diabetes, coronary thrombosis, and so forth. In any study of occupational causes of cancer, the patients who were cured are obviously quite as important as the ones who died of this disease. And finally, the occupation is usually stated in such general terms that it is extremely difficult, if not impossible, to know what the person's environmental exposures really were. Unfortunately, official records, generally, fail to give sufficiently precise data as to either occupations or occupational exposures. Even hospital records are no better, in most cases. The seriousness of this situation from the standpoint of any study of occupational cancer cannot be overemphasized.

Information that a man was a garage worker, for example, provides very little indication as to what he actually did there, or the kind of garage it was. If he worked in a garage where cars were merely parked and stored, his exposure was primarily to carbon monoxide gas in varying concentrations. If, however, he worked in a garage which housed commercial buses carrying diesel engines, his exposure to carbon monoxide gas was relatively less important than was his exposure to aldehydes in the exhaust gases. Aldehydes, though not as toxic as carbon monoxide gas, are highly irritating to the upper respiratory passages. Or, he may have been working in a garage which did repair work. In that case, if he did welding on car bodies, his exposure was very different from what it would have been had he done spray painting.

Similarly, to say a worker is a "foundryman"—a very common designation, by the way—is not sufficient. It makes a great difference whether he is a moulder who handles foundry sand and parting compounds; whether he pours the molten metal, and if so, whether the metal he is pouring contains lead or other toxic materials; whether he sandblasts the finished castings or whether he operates the crane in the foundry. Thus, data as to a worker's occupation must be very precise and very specific in order to provide useful information. Frequently the worker, himself, is unable to provide all of the necessary data because of his lack of technical knowledge—particularly where industrial chemicals are concerned.

For these many reasons, the New York State Occupational Cancer Committee has undertaken to work with live cancer patients, as they come into the hospital for diagnosis and treatment rather than with official records of any kind. Each patient is interviewed in the hospital, and a very long and detailed occupational history taken, starting with his present work and going all the way back to his first job; inquiring how long he worked at each one of his jobs, and the environmental conditions under which he worked, insofar as he can recall. Because of the technical nature of the information to be obtained, it is clear that the patient will not always know the names of the chemical substances he handled in the course of his work; nor will he be able to describe his many occupational exposures in technical terms or interpret dosage. However, if one gets from him *very precisely* the type of work he was doing in each occupation, it is possible for those who are specialists in the field of industrial hygiene to know, from their experience, the chemical and other environmental exposures usually involved in this type of work.

And so, in New York State, the Occupational Cancer Committee has been supplementing the data given by each patient, with reference to each of his occupations, with information as to the environmental exposures known to be associated with those occupations. A statistical analysis of this data, by the use of tabulating machines, is expected to provide leads which can then be studied more intensively in the field.

Clearly, in this type of approach, one is introducing a great many variables—the many jobs held by individual workers; duration and intensity of exposure in each job; the great number of industrial chemicals and other environmental factors; and necessarily the degree of professional interpretation where the patient's information is limited. But these variables, troublesome as they are to the statisticians, are not created by this method of approach. They are inherent in the material under investigation, and one cannot close one's eyes to them. In order to obtain data which may be considered statistically significant, however, under these circumstances, a large series of cases is required. In the present study, an effort is being made to interview 6,000 patients at Roswell Park Memorial Institute in Buffalo. Out of this number, it is anticipated that there will be approximately 1,000 "Normals", i.e. patients who come to the hospital thinking they have cancer but who turn out not to have it.

(CONTINUED IN THE MAY ISSUE)

here, as to whether, in the conjugation of chemical substances by the liver, a particular metabolite in a particular situation may not actually turn out to be more toxic than the original exogenous substance from which it was derived; or can it even turn out to be carcinogenic, perhaps, where the original substance was not? In cases of non-occupational aplastic anemia of unknown etiology, the possibility has been seriously suggested that benzol poisoning of purely *endogenous* origin may occur in a particular person as a result of metabolic disturbances.

Dr. Hueper,[1] in his classic volume on Occupational Cancer, presented known and suspected causes of occupational cancer, giving such supporting data as was available at the time. From this, the New York State Occupational Cancer Committee compiled the tables which appear in the Occupational Cancer Manual[2] which was distributed to you at the beginning of this session. You will observe that they include: A description of selected lesions which may be associated with occupational cancer-producing agents and an alphabetical listing of recognized and suspected occupational cancer-producing agents, with sites characteristically affected.

With this material before you, I shall discuss very briefly a few of the better-understood carcinogenic agents responsible for occupational cancer. Aside from scrotal cancer in chimney sweeps, recognition of the role of beta naphthylamine and benzidine in the production of bladder cancer is perhaps the most important, historically speaking. Dr. Gehrman,[3] who did much of the early work in this field, has been largely responsible for the development of present methods for control, both of the manufacturing processes and of the disease itself. The latter includes periodic medical supervision and physical examinations of workers, with cystoscopy for diagnosis and fulguration of lesions for therapeutic purposes. A recent review of the Italian experience by Barsotti[4] and Vigliani presented in 1948 before the Ninth International Congress on Industrial Medicine in London has contributed further data as to the carcinogenic properties of these dye intermediates. In this study, 186 workmen were examined cystoscopically over a period of several years; some repeatedly. The interesting thing about these bladder cancers is that they cannot be differentiated either cystoscopically or under the microscope from non-occupational epitheliomata of the bladder; and they metastasize just as slowly.

A recent study by Dr. Machle,[5] indicating an increased incidence of lung cancer in workers in the chromate-producing industry, has led to further investigations both in the field and in the laboratory. A field study recently conducted in Ohio by Dr. Mancuso,[6] reported at the last meeting of the American Public Health Association, appeared to support Dr. Maechle's thesis. Dr. Baetjer at Johns Hopkins' and Dr. Smith at the Institute of Industrial Medicine, New York University—Bellevue Medical Center, are now working on this problem with animals under controlled conditions.

The relation of asbestosis to lung cancer has been long suspected. Actually, considerable confirmation has recently been provided by the Chief Inspector of Factories in England,[7] in his Annual Report for 1947. During the period from 1924 to 1946 inclusive, there were 235 deaths either caused by asbestosis or in which asbestosis had been established at necropsy. Cancer of the lungs or pleura was found in 31 of these cases or 13.2 per cent, which is very high compared with a general incidence of 1 per cent for cancer of the lungs among all adults examined at necropsy. Moreover, the sex distribution seemed also to suggest the presence of an occupational carcinogen. The histologic character of the cancers—squamous cell, instead of adeno-carcinoma—and their histogenic derivation, in that the bronchial mucosa was involved rather than the alveolar epithelium, was interpreted to indicate the presence of a specific exogenous carcinogenic agent as the etiological factor; in this instance, inhalation of asbestos dust.

It has been estimated that 20,000 workers are now employed in asbestos-producing industries in this country and Canada. The development of cancer of the lungs in these workers is believed to be more directly related to asbestosis, the disease, than to the inhalation of asbestos dust per se. Differential diagnosis by X-ray between asbestosis and lung cancer presents all the difficulties one would anticipate. It has been suggested that cytological examination of the bronchial secretions might well be included in periodic examinations of workers exposed to asbestos dust whenever clinical or X-ray evidence suggests the possibility of a pre-cancerous lesion. Careful histological studies of lung tissue, postmortem, in all such cases would provide valuable data.

Recent preliminary studies of male pharmaceutical workers engaged in the manufacture of estrogens [8,9,10] would seem to provide additional evidence of a relationship between estrogens and breast cancer. Without being conclusive, these data tend, nevertheless, to add further weight to present concepts that caution is required in the continuous use of estrogens, for any purpose, over long periods of time.

As everyone knows, there has been a dramatic increase in exposure to radiation in industry in recent years—mostly in fields other than radium dial painting. These include the use of X-ray and radium in foundries for the examination of flaws in castings; the use of fluoroscope not only in shoe stores, but in shoe factories to detect misplaced nails in shoes; or as a means of detecting foreign bodies in any packaged goods, including food; the use of radium-coated bars as static eliminators to prevent fire hazards in publishing houses, the manufacture of plastic fabrics, and the like.

These are a few examples of specific chemicals or environmental exposures in industry which, there is reason to believe, could be responsible for the development of occupational cancer unless adequate controls are provided. Are there other substances or other environmental conditions which are not even suspect at present?

The National Cancer Institute, by Grants-in-aid to States, is making possible a more intensive investigation of the whole subject of occupational cancer than has ever before been attempted. And the various States, through their Divisions of Industrial Hygiene, have been approaching the problem differently—each according to its own ideas. A series of pilot studies are thus in progress which, it is anticipated, will not only provide additional data, but will also provide experience with the